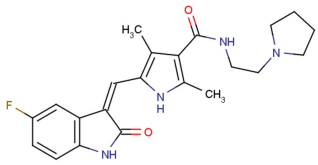
Data Sheet (Cat.No.T13178)

TargetMol
A DRUG SCREENING EXPERT

Toceranib

Chemical Properties



CAS No.:	356068-94-5
Formula:	C22H25FN4O2
Molecular Weight:	396.46
Appearance:	yellow to orange
Storage:	0-4℃ for short term (days to weeks), or -20℃ for long term (months).

Biological Description

Description	Toceranib phosphate is an orally active inhibitor of tyrosine kinase (RTK) receptor, and it potently inhibits PDGFR, VEGFR, and Kit(with Kis of 5 and 6 nM for PDGFRβ and Flk-1/KDR, respectively), has antitumor and antiangiogenic activity.
Targets(IC_{50})	PDGFRβ: 5 nM (ki) Flk-1: 6 nM (ki) PDGFR;VEGFR;Kit: None
In vitro	Toceranib is a selective the tyrosine kinase activity of several members of the split kinase RTK family inhibitor, including PDGFR and Flk-1/KDR(Kis of 5 and 6 nM, respectively)[1]. To explore mechanisms of acquired Toceranib (TOC) resistance in canine MCT, three resistant sublines are generated from the Toceranib-sensitive exon 11 ITD c-kit mutant C2 cell line designated TR1, TR2, and TR3. Growth of the parental C2 cells is inhibited by Toceranib in a dose-dependent manner with an IC50 of <10 nM. In contrast, TR1, TR2, and TR3 sublines are resistant to inhibition by Toceranib (IC50> 1,000 nM). Sensitivity to three other KIT RTK inhibitors is similar to the observed resistance to Toceranib. The parental line as well as all three sublines retains sensitivity to the cytotoxic agents vinblastine (VBL) and CCNU. Following 72 hr culture in the presence of increasing concentrations of Toceranib, treatment naïve, parental C2 cells detach from the culture flask and become rounded, shrunken, and clumped with increased exposure to Toceranib[2].
In vivo	Administration of toceranib significantly decreased the number and percentage of Treg in the peripheral blood of dogs with cancer. Dogs receiving toceranib and CYC demonstrated a significant increase in serum concentrations of IFN-γ, which was inversely correlated with Treg numbers after 6 weeks of combination treatment[1].

Solubility Information

Solubility	DMSO: 2.4 mg/mL (6.05 mM) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.522 mL	12.612 mL	25.223 mL
5 mM	0.504 mL	2.522 mL	5.045 mL
10 mM	0.252 mL	1.261 mL	2.522 mL
50 mM	0.05 mL	0.252 mL	0.504 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. The storage conditions and period of the stock solution: - 80 ℃ for 6 months; - 20 ℃ for 1 month. Please use it as soon as possible.

Reference

1. Mitchell L, et al. Clinical and immunomodulatory effects of toceranib combined with low-dose cyclophosphamide in dogs with cancer. J Vet Intern Med. 2012 Mar-Apr;26(2):355-62.
2. Halsey CH, et al. Development of an in vitro model of acquired resistance to toceranib phosphate (Palladia?) in canine mast cell tumor. BMC Vet Res. 2014 May 6;10:105.
3. London CA, et al. Phase I dose-escalating study of SU11654, a small molecule receptor tyrosine kinase inhibitor, in dogs with spontaneous malignancies. Clin Cancer Res. 2003 Jul;9(7):2755-68.

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